BULLETIN
OF
THE JOHNS HOPKINS HOSPITAL

(THE PUBLICATION OF THE MEDICAL SCHOOL AND HOSPITAL)

(SUPPORTED BY THE DE LAMAR FUND OF THE JOHNS HOPKINS UNIVERSITY)

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July, 1935

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Medical
Faxon

RÔLE OF THE NURSE IN THE CONTROL OF TUBERCULOSIS[1]

WILLIAM H. WELCH, M.D.

Ladies: I have indeed a very great interest in nursing as a profession. My relations date back over thirty years, to the time of my lectures to the nurses at Bellevue Hospital, when I was house physician there. Those were the days of Sister Helen. I don't know whether her name is familiar to nurses in this country, but she did a good deal to advance the cause in England. Here at the Johns Hopkins, my duties have not brought me into close relations with the work of the nurses; nevertheless, my interest has always continued and once in a while I have had an opportunity to demonstrate it, and I assure you it is a great gratification to me to be here today.

It was suggested that I might say something to you about the work of the Committee of One Hundred. It seemed to me that I could hardly fill my allotted time with the few words which I thought would interest you on that particular topic, but the choice of this theme indicates, I think, an interest on the part of nurses in the whole field of public hygiene and preventive medicine; and it occurred to me that I might talk to you about the relation of the nurse to this great line of activity. Of course, your training, like the training of the physician, must relate mainly to the treatment of individual cases of disease. It is your life-work, as it is the life-work of the physician. Nevertheless you doubtless appreciate, to some extent at least, as physicians do—although I don't say that it is adequately appreciated by any large body in the community—that the greatest triumphs of medicine are in the field of preventive medicine—that is, in the effort to check the simply incalculable waste due to sickness and death. We believe that the nurse has a part to play—how large a part is at present

[1] This informal address, taken down by a stenographer, was delivered by Dr. Welch before the Nurses' Alumnae Association, Baltimore, February 4, 1908. It was not edited by the author.

hardly appreciated by nurses themselves—in future developments along these lines. I think it is important that physicians should begin to indicate the directions in which the nurse can be of the very greatest usefulness in public hygiene. The activities in this field are constantly increasing, and one indication is the formation of this Committee of One Hundred. A few words about the origin and present condition of this committee may interest you.

It started a year ago last summer, in June 1906, at the semiannual meeting of the American Association for the Advancement of Science, held at Ithaca, New York. This Association is not composed of medical men alone, but represents primarily the interests of science in all its branches—physics, chemistry, zoölogy, and so on. It has, however, a section of experimental medicine, devoted to the interests of men particularly interested in this field. For reasons I have never been quite able to grasp, I happened to be President of the Association at that time. I was in Albany when the Association met and chanced to attend a meeting of the Section of Economics and Social Science. At that meeting, a very notable paper was read by Prof. Norton, of Yale University. It interested me immensely that an economist and not a physician, in studying the problems which pertain to his field, realized that there was simply an incalculable waste of life, of health and of productive energy from preventable sickness and death and the preventable causes of deteriorated health and energy. He approached the problem not from the medical but from the economic side. This indicated, at least, that economists were beginning to realize, as physicians have long since realized, that there is an enormous waste from disease which can be prevented.

After the reading of this paper, a small committee was appointed to try to mobilize, as some sort of activity, the results which had been brought forth by Prof. Pease; and that little committee, which primarily was simply a committee of the Economic Section of the American Association for the Advancement of Science, grew, in the course of a few months, into what is now known as the Committee of One Hundred. Prof. Pease's paper was published in the *Journal of the American Medical Association* for September 29th, 1906. It is a plea for the establishment of a National Department of Health, and calls attention to the fact that we have no adequate national organi-

zation of public health. All that exists in this country approaching such an organization is the so-called Marine Hospital Service, which has been expanded and is now designated as the Public Health and Marine Hospital Service. This merely assumes *de facto* the functions of a public health organization, but no plans or researches for the work of this bureau have been made to meet in any adequate way what our country ought to do in the prevention of disease and the preservation of health. Prof. Pease called attention to the large funds—many millions—that are expended for the study of prevention of disease in animals. One can get any amount of money for the study of diseases of swine, of cattle; but the Government has never spent a cent for the study of diseases and the prevention of diseases in the human being. England, Germany and France have suitable national organizations and do splendid work in this field. True, our form of government is such that the National Government cannot have very many administrative functions—these must pertain mainly to the separate States and municipalities. Still, there are a great many directives in which a national department or bureau could be of tremendous service. Take, for instance, such a detail as the methods by which Chicago disposed of her sewage, by emptying the refuse and waste material of the whole city into the Mississippi River. If we had had a national bureau or department of health to advise in regard to such matters and stir up public sentiment, I don't for a moment believe that any such unhygienic procedure would ever have been attempted.

This Committee of One Hundred consists, to a very large extent, of laymen. Of course there are many physicians on it, but the movement was initiated outside of medical circles; and it has always seemed to me rather desirable that the main strength of such a movement should be within the lay-public. Physicians themselves do not need to be awakened so much; they are more or less aware of the importance of this question. The lay-public, however, does need to be awakened, and it is interesting that men like Prof. Eliot, Mr. Choate and the President of the United States have lent their support to this great movement. I mention President Theodore Roosevelt among others. He is undoubtedly in sympathy with the work, and wrote a letter to Mr. Irving Fisher, chairman, endorsing the movement, provided it

did not take one specific direction, namely, that it did not ask for a Department of Public Health. This would mean the addition of a new member of the Cabinet, that is, a Secretary of Public Health. We physicians, of course, think that public health is important enough to require a department and a secretary, but the whole sentiment of official circles in Washington, from the President down, is opposed to our asking for such a department. It seems therefore expedient—not, I think, wisest in the broadest sense, perhaps, but expedient—to go no further than to ask for a Bureau of Public Health; for it is understood that if the movement or agitation follows the broader trend of a Department of Public Health, the official support will be withdrawn. You can understand that many physicians are not altogether satisfied with this, but it seems wisest for the present to try to get what we can and not risk an attainable ideal by asking for what at present appears to be entirely unattainable.

Those interested in the work of this Committee of One Hundred have very broad views as to the scope of the work. They are already making efforts to have a smaller committee, which shall prepare articles suitable for publication in newspapers and magazines. Of course, it is simply dreadful, the sort of sensational stuff that appears in the daily newspapers relating to medicine; and partly I suppose for this reason and partly for certain ethical scruples, physicians, generally speaking, are disinclined to have their names attached to statements or articles in the daily papers calculated to educate the public in matters of hygiene. There had existed previously a so-called Public Health Defense League in New York, started mainly to counteract the charlatanry in practice there, the use of proprietary and patent medicines; and to try to bring to trial and conviction, if possible, those who were practising medicine without a license. But this League has really become absorbed by our Committee of One Hundred, so that the membership now of this whole body is something between two and three thousand, with headquarters in New Haven. Prof. Irving Fisher, whose name is doubtless familiar to you on account of his interest in the question of diet, is chairman, and a most active member of the committee; and Dr. Norton, whom I have mentioned before as reading a paper in Albany last summer, is a salaried secretary and executive officer. They have already sent out

a great deal of literature. Their effort is to try to stir up the public in general as to the needs of public health, with the ultimate purpose of securing more and more improvement in the national organization of health in Washington.

There are one or two other organizations, besides the Committee of One Hundred, through which public education about public health is forwarded in this country. One is the work of the American Medical Association. That Association, you know, represents the entire medical profession of this country. In the last five or six years, a kind of reorganization has gone on and the medical profession is now wonderfully well and effectively organized and can accomplish a great deal more than was formerly thought possible. The American Medical Association employed Dr. McCormick—a Kentuckian, with all the gifts and eloquence of a Kentuckian—for this purpose; and he has been most efficient in carrying on this work of reorganization, travelling from state to state in this interest. But Dr. McCormick's work has also taken a more public direction; he is now speaking to lay as well as to medical audiences. His work is now largely educational, reaching the general public. He frequently "legislates," speaking before the legislatures of the different States, and always with such eloquence and force that he is making a very great impression. Possibly the American Medical Association could do nothing better than to keep Dr. McCormick as a public educator—a rather gradual evolution from the sort of work he was first called upon to do.

There is a third movement relating to this whole question of public health that may interest you. I have spoken of the Committee of One Hundred and of the work of the American Medical Association through Dr. McCormick, and now I mention the effort that is being made to reach the people at large, by popular lectures relating to such problems of disease and of health as seem important enough to be taught to the public. Professor Eliot, in an admirable address delivered at the dedication of the new buildings of the Harvard Medical School—those splendid, unrivalled buildings in Boston that doubtless many of you have seen—emphasized above all else the importance of the physician's rôle in instructing the public as to right ways of living —healthy living. He said that he believed the work of the physician in the future will be in many respects different and in many respects of a

higher order than in the past. Partly as a result of that very eloquent appeal—again from a layman and not from a strictly medical source—partly as a result of that address, the Harvard Medical School established weekly lectures for the public on topics concerning disease and health. They were held in the Harvard Medical School and were largely attended, arousing a great deal of interest in the community. And now the Medical and Chirurgical Faculty, our State organization in Maryland, is adopting very much the same plan. Under conditions here in Baltimore, it seems preferable that this campaign of education should be conducted under the auspices of our State Medical Society rather than under the direction of any particular medical school or any body narrower than the State Faculty. These lectures are held every Saturday evening and afford, I think, another illustration of this great interest and desire to arouse the public.

Of course, you are interested mainly in the share which nurses are going to take in this movement. There are many activities that can be pursued far more effectively by nurses than by any other members of the community; they are the ones who are going to carry the message of health into the homes; they are the ones who are going to come into most direct contact with those who most need instruction. I do not think we as yet appreciate what a field of really unsurpassed usefulness is going to open to nurses in this direction; and nothing illustrates this better than the problem of tuberculosis.

Quite recently I had the privilege of attending a large public meeting in Albany, the purpose of which was to stir up the interest of the public in the campaign against tuberculosis in the State of New York. The city of New York has been very active in this direction—indeed, in many respects it has taken the lead for the whole world in the movement against tuberculosis; but New York State has been very slow to follow its lead. This public meeting was called when The State Medical Society was meeting in Albany and also at the time of the session of the Legislature. Mr. Choate, was chairman of the committee, and Mr. Hughes, the Governor of the State, gave one of the most notable addresses. It was an inspiring occasion. Even the aisles of the large hall were filled. There was a large crowd outside that could not be admitted, and Mr. Choate opened his remarks

by saying that although the struggle against tuberculosis was being actively carried on, the struggle to get into the hall was even greater.

I used the opportunity afforded me on this occasion to say something about what can be expected from application of existing knowledge to practical measures in the movement against tuberculosis. This put me in the somewhat embarrassing position of prophesying as to the future; but while I do not care to be too definite as to exact figures, I think it fair to say that with application of entirely reasonable and practicable measures the amount of tuberculosis can be reduced at least one-half within the next two decades; based, of course, upon the advances made since the discovery by Koch, in 1882, of the tubercle bacillus. We know the germ, we know how it is eliminated from the body, we know the sources of infection; and if the knowledge we now possess is intelligently applied, we can confidently predict very important results in the prevention of the disease. There has been a notable diminution of tuberculosis in certain countries; and if one studies existing conditions, he will reach the conclusion that these are the countries in which preventive measures have been most actively applied. Perhaps the largest reduction is effected in Prussia, where, today, a most efficient campaign against tuberculosis is going on. They have a sanatorium that will accommodate over 2500 tuberculosis patients, at least 2500 are treated annually; and when you consider that this represents about one fourth of the total mortality from tuberculosis, you can see how far ahead of us they are in this one particular. But the fact that we are getting notable results, even by inadequate and imperfect application of preventive measures may encourage us to consider what might be expected if we could proceed more efficiently.

I would put first among these measures the notification and registration of the disease. It is singular that some physicians object to the passing of such ordinances or laws. There has been a great deal of discussion on this matter and there are not many places where it is effectively carried out. But I regard notification to the Health Authorities as the first step in the fight against any infectious disease; for only in this way can we proceed efficiently to prevent its spread. And so I would emphasize the importance of notification and registration of cases of tuberculosis on the part of physicians and others.

Secondly, there should be means available for early diagnosis. We know today that tuberculosis is not only preventable but that it is also curable, although curable only when appropriate measures are taken in the early stages of the disease; and we know that the earlier the treatment, the more favorable the results will be. It is therefore self-evident that means should be provided by which early diagnosis can be made. Diagnosis today is carried out largely by laboratory methods—examination of the sputum, the use of tuberculin, and so forth. You, see at once, how necessary is the establishment of laboratories, supported by the municipality and the State, where physicians can have such examinations made free of charge.

The greatest interest, of course, attaches to special institutions to be erected or employed for the prevention of the disease—the sanatorium, the hospital for advanced cases, and the special tuberculosis dispensary. Now as regards sanatoria—they undoubtedly take the first place in the treatment of tuberculosis, and a preventive movement in any community usually starts as an effort for the establishment of sanatoria. In this State, we are very fortunate to have secured a good appropriation from the Legislature for the establishment of a model institution of this kind. It is impossible, I think, to overestimate the usefulness of the sanatorium for the treatment of early cases; but it is a mistake to give it the foremost position in a campaign for the prevention of the disease. Not, for a moment, would I say anything against the establishment of the sanatorium, but merely indicate what I conceive its position to be in the campaign. In the main, of course, it takes in the early cases for treatment, but to no great extent do these supply the probable foci in the spread of the disease. These early cases are often not eliminating tubercle bacilli at all; indeed, we make a sharp distinction between open and closed cases of tuberculosis. The open case implies that the patient is discharging tubercle bacilli, chiefly through the sputum. In the closed case the patient has tubercle bacilli in the lungs, but is not discharging these bacilli in the sputum, and is therefore not a source of danger to others. Now the more of these closed early cases of tuberculosis we can recognize and send to sanatoria, the more effective will the sanatoria be in prevention. When the sanatorium takes in as many patients in this country as in Germany, then will it occupy a

position of the very greatest importance; and every effort should be made, I think, toward the establishment of more and more of these institutions and to have more and more patients in the early stages of the disease inside them for treatment.

It is the hospital for advanced cases of tuberculosis that I would put first in importance in the preventive scale,—of course, not as to treatment, for only a relatively small number of such patients can be benefited by treatment. The establishment of a sanatorium is much easier to effect than the establishment of a hospital. It makes a stronger humanitarian appeal when you can say that the sanatorium will afford means of recovery; whereas the hospital does not hold out much hope of cure. The sanatorium makes this strong appeal, but those who have paid closest attention to the problem of prevention are convinced, I think, that the hospital represents the important factor in prevention of the disease. More and more patients should be induced to go to these hospitals—taken out of their homes, often in the crowded unsanitary quarters where so many of them live, so that the rest of the family are protected from infection at that source.

Prof. Koch puts the hospital for advanced cases first in importance. He holds that results attained in Prussia, Stockholm and England for over fifty years are to be interpreted by the fact that, in these countries, hospitals for advanced cases exist and treat many patients.

The problem is to make such hospitals more attractive. Without going into details, I say that one of the most important questions is the establishment of suitable hospitals for cases of tuberculosis in advanced stages of the disease, suitably located, with bright and attractive surroundings

It is estimated, today, that not more than 2 to 4 per cent of all cases are treated in public institutions—that is, 96 to 98 per cent of tuberculosis patients are outside of such institutions; and the great problem, I think, is how are they to be reached; for these are the patients who are in their homes or crowded workshops. This problem has been handled with a large measure of success by the establishment of the special tuberculosis dispensary, and in this dispensary, the nurse, or the visiting nurse, is the most important part of the machinery. The nurse goes into the home and instructs the patient how to guard against spreading the disease and thus protects the

other members of the family. When there is a case of tuberculosis in a home where there are children, you can count almost certainly upon some of those children being already infected; and these, above all, should be examined. Often, in such cases, one finds the very beginnings of the disease. Such children can be taken to sanatoria and cured. I cannot emphasize too much my conviction as to the importance of the special tuberculosis dispensary and its increasing value in the future. The Germans, I may say, have a more fortunate name than our word "dispensary." They call it a *Beratungsstelle*, a place for information, aid and advice. They lay the least stress upon methods of treatment; they stress the dispensary mainly as a scientific center for the prevention of disease and especially for giving advice and reaching early cases. I put, therefore, this so-called "dispensary," with its machinery of nurses and health inspectors, as is the case in New York, in the very first rank among measures for the prevention of the disease.

While the work of the nurse in hospital and sanatorium is very much as heretofore, there is in the dispensary a very special field of work which is absolutely essential for carrying out these measures efficiently. Viewed as an international problem—the prevention of the disease for the good of mankind—looked at from this broad point of view this should be one of the main fields of endeavor in our State Health Departments. And in this regard, we are far behind the rest of the world. Dr. Osler has stated that nothing impressed him so much as the difference between England and America in matters of public health. No one in England, even in a small town, holds the position of health advisor unless he has had special training in public hygiene.

I do not see how things can go on much longer without improvement—a broader field of activity, a more public recognition of the importance of special training for our sanitary advisors, and of the need for a larger appropriation and a larger force. Every Department of Health should have associated with it an official tuberculosis bureau, its personnel giving their whole time to this question.

Naturally, there are other important points in connection with this work that I might touch upon—the disinfection of houses occupied by patients, or where there has been a death or removal, and so on—but it is impossible to go over them in detail. What I particularly

wish to leave with you is this one illustration of the opportunities open to the nurse and the demand which the future, in greater measure than today, is going to make upon her in this particular field. I cannot understand the agitation about nurses being over-trained and over-educated. In New York it is a backwoods and benighted sentiment to maintain that knowledge, under any circumstances, is dangerous; and the more training and the more knowledge the nurse has acquired, the more valuable she will be in this great work.

EFFECTS OF THE INTRAVENOUS ADMINISTRATION OF HYPERTONIC SOLUTIONS OF SUCROSE

With Special Reference to the Cerebrospinal Fluid Pressure

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In a recent study (1), evidence was presented to show that when a hypertonic solution of dextrose in effective amount and concentration is injected intravenously into a human subject for the purpose of reducing intracranial hypertension, the desired diminution in the pressure of the cerebrospinal fluid may be followed by a period of increased intracranial pressure and a number of unfavorable clinical signs and symptoms. In an attempt to find a non-toxic substance whose osmotic action in the circulation would not be complicated by these adverse sequelae, the physiological effects of the intravenous injection of hypertonic solutions of sucrose[1] were investigated in 35 human subjects according to the following technique:

MATERIAL AND METHODS

Ward patients between 18 and 40 years of age and free of determinable organic disease were chosen for this study. Each subject was given 10 grains of barbital to promote relaxation, and his colon and bladder were emptied. He was then allowed to rest in bed for half an hour, his control pulse rate and blood pressure being determined at the end of this period. Lumbar puncture was done under local anesthesia; 5 cc. of spinal fluid were collected and a water manometer

[1] This study was begun after hearing Dr. M. I. Gregerson of Harvard report some unpublished preliminary studies on the effects of the intravenous administration of hypertonic solutions of sucrose in dogs.

attached to the lumbar needle. By means of special pillows and the renewal of the local anesthesia, the patient could then be kept relaxed and comfortable in a lateral position for several hours of continuous observation.

Manometric readings began with an initial period of 20 to 60 minutes during which the subject's cerebrospinal fluid pressure was observed to establish itself at a stable "basic" level.[2] A control sample of 20 cc. of blood was then removed from a cubital vein and the subject given various amounts of a 50-per-cent solution of sucrose[3] intravenously at rates of 5 to 10 cc. per minute. During the injection

[2] For control observations as to the relative stability of the "basic" pressure of the cerebrospinal fluid in the human see Masserman, J. H.: Cerebrospinal Hydrodynamics IV, Clinical Experimental Studies, *Arch. Neurol. and Psychiat.*, **32**: 523, (Sept.) 1934.

[3] In the earlier studies, a 50-per-cent solution of sucrose furnished in 100 cc. ampoules by Eli Lilly and Co., Indianapolis, was used. This preparation contained about 0.25 per cent of reducing substance when tested with Benedict's solution, but was otherwise satisfactory. For our later work, the solutions of sucrose for intravenous use were prepared in our own laboratory as follows: Domino Granulated Table Sugar was purchased on the open market and dissolved in twice its weight of freshly distilled water. This solution was immediately filtered, placed in cotton-stoppered 1000-cc. flasks, sterilized in a boiling water-bath for 3 hours and cooled to body temperature for injection. One hundred cubic centimeters of a solution prepared in this manner produced no subjective or objective ill effects when administered intravenously to the author.

The freshly sterilized preparation gave no test for reducing sugars with qualitative Benedict's solution. However, at 24 hours a heavy trace of reducing substances was present, and at 48 hours these had reached a concentration of about one per cent. Although the presence of even this admixture of monosaccharides would, theoretically, not significantly impair the efficacy of the sucrose, nevertheless it was judged advisable to use the solutions as soon after sterilization as possible, and this was done in every case. As to other possible impurities in the solutions, Mr. Louis A. Wills, technologist to the American Sugar Refining Co., gives the following analysis of the sugar employed in their preparation:

(Sucrose: approximately 99.97 per cent)

"1. Reducing sugar—0.002 to 0.02%, consisting of a mixture of dextrose and levulose with the former probably predominating.

"2. Ash—0.002 to 0.01%. Not even the slightest traces of heavy metals have ever been detected to our knowledge.

"3. Barium and Arsenic. Absent even in the slightest traces to the best of our knowledge."

and for 4 to 6 hours thereafter, readings of cerebrospinal fluid pressure were taken about every 10 minutes, the pulse rate and blood pressure were checked every half hour, and at appropriate periods specimens of urine, blood and spinal fluid were collected for cytologic and chemical study. In 12 cases, moreover, spinal and/or cisternal punctures were repeated at 8 and 24 hours after the injection of the sucrose, in order to determine the composition and pressure of the cerebrospinal fluid at these intervals. Finally, the clinical condition of the subject was followed closely throughout the experiment and for several days thereafter.

RESULTS

Clinical effects. As a preliminary to the experimental work, the author received an injection of 100 cc. of 50-per-cent sucrose intravenously. There was no pain at or about the site of the injection following the needle puncture, and the only effects noticed subsequently were a rather pleasant sensation of warmth during the injection and a mild diuresis thereafter.

In about two-thirds of the subjects investigated, flushing of the skin was observed during the injection of the sucrose, and 3 of the 17 subjects who received as much as 500 cc. of the 50-per-cent solution complained of vague discomfort in the lumbar region while it was being administered. In one instance in which an estimated 5 to 10 cc. of the solution accidentally escaped into the tissues about the vein, there was a mild periphlebitis and an oral temperature of 99.8°F. lasting about 8 hours. No undesirable clinical effects were noted in any other case in our series.

Effects on cerebrospinal fluid pressure. The average deviations in the pressure of the cerebrospinal fluid resulting from the intravenous administration of various amounts of a 50-per-cent solution of sucrose are plotted in figure 1. To summarize the data: The injection of 100 cc. or more of the solution caused an initial rise in the pressure of the cerebrospinal fluid, which persisted for from 20 to 80 minutes after the beginning of the injection. When 300 cc. of the solution were administered, the cerebrospinal fluid pressure subsequently dropped to 21 to 76 mm. of water (average 40 mm.) below the base line, and then slowly mounted to its original level. When 500 cc. of the

50-per-cent solution were administered, the fall in spinal pressure that succeeded the initial rise ranged between 75 and 140 mm. and persisted for two and a half hours or longer before regaining basic level. After this, there were varying periods of mild cerebrospinal hypertension in 5 of the 17 subjects given this amount of sucrose, but in no instance did the spinal pressure rise more than 18 mm. above normal, whereas in 5 cases the pressure had not regained its original

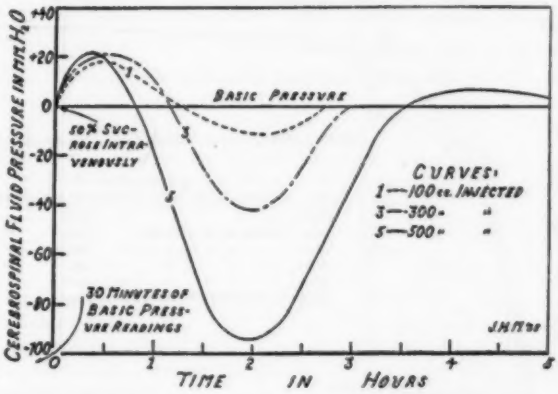

FIG. 1. AVERAGE DEVIATIONS OF THE PRESSURE OF THE CEREBROSPINAL FLUID IN 31 HUMAN SUBJECTS DURING AND AFTER THE INTRAVENOUS ADMINISTRATION OF VARIOUS QUANTITIES OF A 50-PER-CENT SOLUTION OF SUCROSE

Curve 1, 7 cases; curve 3, 7 cases; curve 5, 17 cases. Although the data in each series are not sufficiently numerous to warrant explicit statistical derivation, the respective curves nevertheless represent deviations of such relative constancy as to render the experimental results clinically significant.

level at the end of the 5-hour period of continuous observation. This mildness or absence of a reactive intracranial hypertension was, therefore, in marked contrast to the secondary osmotic effects produced by the intravenous administration of dextrose, as reported in a previous paper (1).

Urinary excretion (*fig. 2*). The intravenous injection of 100 cc. or more of a 50-per-cent solution of sucrose caused a marked and prompt diuresis in every case investigated; in 17 cases, the mean output of

urine within 4 hours after the injection of 500 cc. of the solution (fig. 2, curve A_5) approximated 2300 cc. It is interesting to note that this amount of urine contained an average of 63 per cent of the sucrose administered (curve $\%5$), and that within 24 hours 78 to 92 per cent of the total sucrose could be thus recovered.[4] The administration of smaller amounts of the 50-per-cent solution, of course, induced lesser

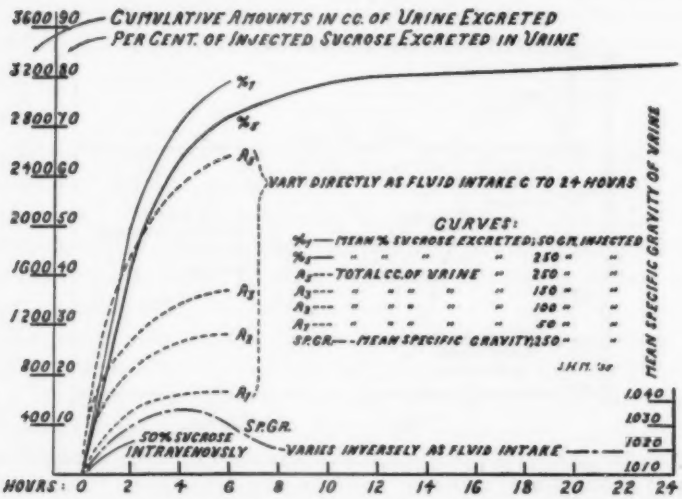

FIG. 2. THE AVERAGE AMOUNT OF URINE EXCRETED AND ITS MEAN CONTENT OF SUCROSE AFTER THE INTRAVENOUS ADMINISTRATION OF VARIOUS QUANTITIES OF A 50-PER-CENT SOLUTION OF SUCROSE TO 35 HUMAN SUBJECTS

Curves $\%_1$ and A_1, 7 cases; curve A_3, 7 cases; curve A_2, 4 cases; curves $\%_5$, A_5 and Sp. Gr., 17 cases.

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[4] To determine the quantity of sucrose in a specimen of urine, 5 per cent of hydrochloric acid was added, and the urine incubated at approximately 37°C. for about 18 hours. The acid was then titrated with sodium hydroxide, the quantity of reducing sugar per cent determined by the use of Benedict's quantitative solution, and the quantity of sucrose originally present in the urine obtained by multiplying the result by 0.96. This method, though largely empirical, gave an error of less than 6 per cent in a series of known controls with a range of concentration of from 1 to 20 per cent.

degrees of diuresis (curves A_1, A_2, and A_3), but resulted in relatively higher initial rates of elimination of the sucrose (curve %1).

The urine in every case remained free of dextrose, albumin and casts when tested by the ordinary laboratory methods.

Blood chemistry. In table 1 are listed the average content of sucrose, dextrose, chlorides and non-protein nitrogen, and the average icteric index and carbon dioxide combining power of samples of blood taken before and at various intervals after the injection of 500 cc. of a 50-per-cent solution of sucrose. The blood sucrose (series 1) was, of course, high immediately after the injection, but declined to levels below the significant threshold of our tests within 8 hours.[5] As to the

TABLE 1

Mean values of samples of blood of 16 patients taken before and at various intervals following the intravenous injection of 500 cc. of a 50 per cent solution of sucrose

NUMBER	BLOOD SERIES	BEFORE SUCROSE	HOURS AFTER INTRAVENOUS INJECTION OF 500 CC. OF 50-PER-CENT SUCROSE				
			½	1	2	4	8
1	Sucrose, mgm./100 cc.	0	660	479	299	27	0
2	Dextrose, mgm./100 cc.	78.3	82.3	80.7	86.6	*	*
3	Non-protein nitrogen, mgm./100 cc.	28.3	*	*	27.4	26.2	*
4	Chlorides, mgm./100 cc.	280	*	*	278	242	*
5	Icteric index	5.3	*	*	5.3	5.4	*
6	CO_2 combining power, volumes/100 cc.	56.6	*	*	62.1	54.3	*
7	Clotting time, minutes	3.9	1.2	1.9	3.2	3.1	*
8	Bleeding time, minutes	2.4	1.2	1.3	1.8	2.8	*

other variables studied (series 2 to 6), the deviations from their respective norms after the injection of the sucrose were too small and

[5] The sucrose content of the samples of blood was determined as follows: To 5 cc. of the protein-free tungstic blood filtrate, 0.5 cc. of concentrated HCl was added, the mixture kept at 37°C. for 24 hours, neutralized with NaOH, and diluted to 10 cc. The total quantity of reducing sugars was then determined by the Folin macro method (Folin, O.: Two Revised Cooper Methods for Blood Sugar Determination, *J. Biol. Chem.*, **82**: 83, 1929). The result was corrected for sucrose by subtracting from the quantity of invert sugar present the dextrose content of the same sample of blood as previously determined, and multiplying the remainder by 0.96. Known quantities of sucrose could be recovered within an 8-per-cent margin of error in control samples of blood tested by this method.

inconstant in direction to warrant specific physiological interpretations at present.

Blood cytology. Contrary to expectations, the intravenous administration even of 500 cc. of a 50-per-cent solution of sucrose did not cause a discernible crenation of the erythrocytes at any time after the injection, nor was there any significant change in the average erythrocyte counts. In 6 of the 17 patients who received this amount of the solution, however, there was a definite reactive leukocytosis reaching its height (12,500 to 18,000 cells) at about 5 hours after the injection. The differential counts at this time were highly variable, ranging from normal configuration to about 80 per cent polymorphonuclear or 60 per cent small lymphocytic cells, the large lymphocyte and eosinophile fractions remaining not significantly altered. Recheck blood counts in all patients 12 and 24 hours after the injection were within the limits of normal.

Bleeding and clotting time. There was a small but fairly consistent decrease in both the average bleeding and clotting time of the blood within an hour after the administration of 500 cc. of 50-per-cent sucrose (table 1, series 7 and 8), but the significance of this observation will have to be checked in a larger series of cases.

Blood pressure and pulse rate. No consistent deviations in these were noted in our subjects at any time following the administration of the sucrose.

Dextrose and sucrose content of the spinal fluid. As may be seen in table 2, the dextrose content of the spinal fluid was not significantly altered by the administration of 500 cc. of a 50-per-cent solution of sucrose. Further, it is important to note that 4 hours after its intravenous injection only a very small quantity of the sucrose—37.6 mgm. per cent—had permeated into the spinal fluid, and that even this amount had been almost completely eliminated from the fluid at the 24-hour interval.[6] The blood-encephalic barrier, therefore, seems

[6] The sucrose content of the samples of spinal fluid was determined as follows: To 5 cc. of the fluid was added 0.5 cc. of concentrated HCl, the mixture incubated at 37°C. for 24 hours, neutralized with NaOH, and diluted to 10 cc. The quantity of invert sugar was then determined according to the method of Folin-Malmras (Folin, O., and Malmras, H.: An Improved Form of Folin's Micro Method for Blood Sugar Determination. *J. Biol. Chem.*, **83**: 115, 1929). The result was then corrected for sucrose as in footnote 6.

relatively impermeable to sucrose—a factor of possible significance in accounting for its apparent lack of toxicity and the absence of marked intracranial hypertension as a terminal effect of its administration.

COMMENT AND CONCLUSIONS

From the foregoing data, it may be inferred that sucrose in 50-per-cent solution, when administered intravenously to human subjects for the purpose of reducing the pressure of the cerebrospinal fluid, has these advantages over corresponding strengths of dextrose[7] or of the electrolytic salts:

1. A 50-per-cent solution of sucrose satisfactory for clinical use may be easily and cheaply prepared.
2. When 300 to 500 cc. of this solution is administered intravenously

TABLE 2

Mean content of dextrose and sucrose of samples of spinal fluid of 16 patients taken before and at various intervals following the intravenous injection of 500 cc. of a 50-per-cent solution of sucrose

MGM. IN 100 CC. OF SPINAL FLUID	BEFORE INJECTION OF SUCROSE	HOURS AFTER INTRAVENOUS INJECTION OF 500 CC. OF 50-PER-CENT SUCROSE		
		2	4	24
Dextrose	56.3	58.2	50.3	48.8
Sucrose	0	37.6	24.7	6.4 to 0

the initial rise of cerebrospinal fluid pressure (probably coincident to the initial increase in blood volume and venous pressure) is of lesser degree and duration than is the case with the dextrose or the electrolytic solutions (1). Subsequently, the desired diminution in intracranial tension (probably resulting from the diuresis and tissue dehydration) (2) is greater and more prolonged.

3. Corresponding to the relative impermeability of the blood-cerebrospinal-fluid barrier to sucrose, there is only a slight and transient intracranial hypertension as the final hydrodynamic effect of its intravenous administration. In contrast to this, dextrose and most of the physiologic salts pass readily from the blood into the central

[7] In this connection, it must be remembered that a 50-per-cent solution approximates in osmotic tension only a 25-per-cent solution of dextrose.

nervous system and the cerebrospinal fluid, and thereby induce, as their terminal osmotic effect, a marked and prolonged increase in spinal-fluid pressure and possibly also an edema of the central nervous tissues (3).

4. A 50-per cent solution of sucrose when administered intravenously does not cause an overt phlebitis in the injected vein, and induces only a mild reaction if allowed to escape in small amounts into the subcutaneous tissues.

5. Comparatively large amounts of sucrose in the circulation are apparently not toxic, and cause no serious disturbances in the chemistry or cytology of the blood.

6. Being a disaccharide and foreign to the blood stream, sucrose is not extracted from the circulation into the tissues (4). Instead, it induces a marked diuresis and is eliminated rapidly in the urine.

7. Since sucrose is thus either completely eliminated or else metabolized in the body only in small amounts (5), repeated injections of sucrose can be given when necessary without cumulative adverse effects.

As to the clinical use of hypertonic solutions of sucrose for the purpose of reducing the intracranial hypertension in patients with cerebral concussion, meningitis, etc., and pre-operatively in cases of brain tumor, it must of course be recognized that the disturbances in cerebral circulation and tissue permeability that obtain in these conditions might modify the osmotic and dynamic effects here reported in normal individuals. Nevertheless, in view of the ready availability and apparent lack of toxicity of the solutions, their administration for their demonstrated decompressive and diuretic effects seems to deserve a careful clinical trial.

The author wishes to express his thanks to Dr. H. Goldsmith, Dr. S. Katzenelbogen and to Dr. S. Diener for their coöperation in this study.

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SYPHILITIC MYOCARDITIS

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It is not unusual, on a large hospital service, to come upon a case of severe cardiac decompensation which cannot be explained in accordance with the commonly accepted causes of heart disease. When such a case is met with in an individual past middle age we are often satisfied to classify the condition as hypertensive or as arteriosclerotic in origin. However, when the patient is young and there is neither hypertension nor evident arteriosclerosis it is not quite so easy to accept such an explanation. During the recent past there have been quite a few such interesting cases observed in the medical wards of the Baltimore City Hospitals.

The upper limit of age of the cases in this study was arbitrarily set at 46 years, so that the picture might not be so obscured by arteriosclerosis and such complications as are more common in those past middle age. In 3000 admissions to the medical wards, there were, within this age limit, 20 cases of unexplained cardiac decompensation. These patients compose a rather homogeneous group and the similarity of one case with another is striking, the histories and physical findings being more or less stereotyped. Of the 20 cases, 16 were in colored males; 2 in white males; and 2 in colored females. It is difficult, in these cases, to attribute the failure of the heart to any of the usually accepted causes of heart disease. In none was there any definite history of rheumatic fever, chorea, or scarlet fever. There was no hypertension, no nephritis and no anginal attacks suggesting coronary arteriosclerosis. By physical findings, there was no evidence of any organic valvular disease: in fact, in some of the cases not even a mitral systolic murmur could be heard. All of the hearts, by percussion and x-ray examination, were enlarged to both left and right. Without exception, all presented protodiastolic gallop rhythms

on admission, and usually the gallop persisted for several weeks. Practically all these patients have been admitted to the hospital several times during the past two years, each time with signs of cardiac decompensation,—dyspnoea, orthopnoea, oedema, enlargement of the liver, and frequently ascites and pleural effusion. All gave positive Wassermann reactions or had previously received antisyphilitic treatment.

The records of those of the twenty cases which have come to autopsy are, briefly, as follows.

Case 1. C. B. Colored male, aged 41.

Admitted 10–9–33, complaining of "swelling of the legs." Penile lesion 15 years before. Antisyphilitic treatment for three years. Treated at the Johns Hopkins Hospital in 1931 and again in 1932 for cardiac decompensation, the etiology of which was by some members of the staff thought to be a syphilitic myocarditis. Fairly well, following second discharge from the Johns Hopkins, until August 1933 when he again became dyspnoeic. Progressive oedema of lower half of body, 3 weeks. "Swelling" of abdomen, 2 weeks. No precordial pain or anginal attacks.

P. E. Dyspnoea. Orthopnoea. Oedema of lower half of the body. No sclerosis of the retinal vessels. Many moist râles at both lung bases. Heart considerably enlarged to both sides. No murmurs heard. Protodiastolic gallop rhythm at apex. B.P. 130/110. Liver 2 f.b. below costal margin.

Urine. S.G. between 1.010 and 1.020; trace of albumin on admission, none on subsequent examinations; a few w.b.c., no r.b.c. or casts. Wassermann test negative.

During the first 15 days in bed he lost 46 pounds in weight, most of which was due to loss of oedema. Systolic blood pressure varied between 130 and 120: the diastolic between 110 and 80. Discharged 7 weeks after admission well compensated. B.P. 120/70. The gallop rhythm had entirely disappeared.

Second admission 2–5–34. Had been well for one month when the old symptoms again appeared and became progressively worse.

P. E. Marked respiratory distress. Many râles over both lung bases. Oedema of lower half of body. Heart greatly enlarged. No murmurs. Constant protodiastolic gallop rhythm. B.P. 130/90. Liver down 3 f.b.

The following day the B.P. was 124/70. Condition rapidly worse. Died 24 hours after admission.

Autopsy. Heart 780 grams. Both ventricles hypertrophied and dilated. No valvular lesions. Chordae tendineae delicate. Some slight thickening of the aorta 5 to 6 cm. above the aortic valves. Numerous gray translucent scars on posterior wall of left ventricle. Coronary arteries delicate and patent. No narrowing of the coronary orifices. Sections show numerous scars, often infiltrated

with round cells. Also, rather marked round-cell infiltration around small blood vessels.

Kidneys show no evidence of nephritis or sclerosis of blood vessels.

Case 2. H. C. Colored male, aged 32.

Admitted 3–28–33 because of dyspnoea and oedema. Penile lesion 12 years before. Bullet wound of left chest, followed by empyema, 3 years before. Apparently complete recovery subsequent to thoracotomy.

P. I. Oedema of feet and ankles, gradually increasing to involve the lower half of body, for three months. Dyspnoea, 6 weeks. No precordial pain or attacks of angina pectoris.

P. E. Well developed colored male of 32 years. Dyspnoea and orthopnoea. Marked oedema of lower half of body. Old thoracotomy scar on left. No sclerosis of retinal vessels. Impaired percussion and diminished breath sounds at base of left chest. Heart greatly enlarged to left and right. Soft systolic murmur at apex. Gallop rhythm. B.P., on admission, 160/120; 2 days later, 135/110. Liver 3 f.b. below costal margin. Moderate ascites.

Urine. S.G. between 1.010 and 1.022; albumin, 0 to 2 plus; occasional hyalin cast and a few w.b.c. N.P.N. 30 mgm. %. Wassermann 4 plus.

On bed rest and digitalis he improved rather rapidly and was discharged 4–29–33, well compensated.

Readmitted 9–26–33. Had been fairly well for about 4 months when the dyspnoea, oedema and swelling of the abdomen returned.

P. E. Marked oedema of lower half of body. Veins of neck quite distended. Dyspnoea. Râles at base of right lung. Heart considerably enlarged to both sides. Short systolic murmur at apex. Protodiastolic gallop rhythm. B.P. 140/120. Liver down 4 to 5 f.b., but not particularly tender.

Urine, not remarkable. N.P.N. 30 mgm. %. Systolic blood pressure varied between 140 and 120: the diastolic between 120 and 110. Gradually became more and more oedematous. Died 12–19–33.

Autopsy. Heart 660 grams. Epicardium and endocardium thickened and opaque in patches. Aortic, mitral, tricuspid, and pulmonary valves delicate. Coronary arteries not sclerotic. No obstruction nor narrowing of coronary orifices. Very little syphilis of the aorta. Sections of the heart show many scars, with clumps of lymphocytes about the small blood vessels and between the muscle bundles. Kidneys and adrenals show no arteriosclerosis.

Case 3. C. J. Colored male, aged 39.

Admitted 7–6–33. Chancre 20 years before. Antisyphilitic treatment 12 years later. General health otherwise rather good.

P. I. Sudden attack of nocturnal dyspnoea, 6 months (Jan. 1933) before admission: awakened with choking sensation. No pain. Similar attack 3 nights later. Oedema of feet for ten weeks.

P. E. Moderately dyspnoeic colored male of 39 years. No sclerosis of retinal

vessels. Lungs clear except for few râles at both bases. Heart enlarged to percussion. Sounds "clear." No murmurs heard. Pulse regular. B.P. 125/60. No sclerosis of peripheral vessels. Moderate pitting oedema of ankles.

Urine. S.G. between 1.010 and 1.023; no albumin; no casts or r.b.c. P.S.P. 60% in 2 hours. Wassermann positive.

Responded well to bed rest and digitalis. Discharged 8–24–33, 6 weeks after admission, well compensated.

Second admission 12–28–33, 4 months after discharge. Had been well until 2 weeks before, when the dyspnoea, orthopnoea, and oedema of the ankles reappeared.

P. E. Dyspnoea and orthopnoea. Marked oedema of the lower extremities. Marked distention of the veins of the neck. Many râles at both lung bases. Heart considerably enlarged. Sounds distant. Faint systolic murmur at apex. Protodiastolic gallop rhythm. B.P. 150/120. Two days later, 130/86.

Urine not remarkable. Moderate anaemia. Wassermann positive.

Again improved rapidly on bed rest and was discharged 1–27–33, well compensated.

Third admission 2–25–34, one month after second discharge, complaining of hiccup for two days. Temperature ranged between 102.4° and 104.4°F. Respirations between 26 and 40. "Rusty" sputum. Consolidation of upper lobe of right lung. B.P. 100/60. No evidence of cardiac decompensation. Died, 3–1–34, of lobar pneumonia.

Autopsy. Heart 515 grams. Epicardium opaque. All valves delicate. No typical syphilis of the aorta. Numerous scars in the myocardium associated with infiltration of lymphocytes. No sclerosis of the coronary arteries and no narrowing of the orifices.

Upper lobe of right lung consolidated. No definite nephritis, although a few of the smaller arteries of the kidneys and pancreas show slight hyalin changes.

Case 4. G. S. Colored male, aged 46.

Admitted 12–13–33 complaining of "shortness of breath." Gonorrhea 8 years before. Chancre 7 years before. Otherwise health had been rather good.

P. I. Vague feeling of discomfort in chest, while working, three weeks before admission. Next day he became dyspnoeic. Some coughing, with blood-streaked sputum for ten days.

P. E. Dyspnoea. Orthopnoea. Paroxysms of coughing. Bloody sputum. No sclerosis of retinal or peripheral vessels. Many râles at both lung bases. Heart enlarged to left and right. Systolic murmur at apex. Protodiastolic gallop rhythm. B.P. 145/80. Slight pitting oedema of ankles.

Wassermann positive. Urine not remarkable. N.P.N. 30 mgm. %.

Left the hospital against advice, eleven days after admission, so that he might be home for Christmas.

Readmitted 2–7–34. Paroxysms of dyspnoea had returned about one week

after he had left the hospital. Remained in bed for two weeks with some relief. Attacks of dyspnoea more frequent and more severe.

P. E. Marked dyspnoea. Orthopnoea. Râles at both lung bases. Heart considerably enlarged to both sides. Blowing systolic murmur at apex. Protodiastolic gallop rhythm. B.P. 140/80. Liver down 2 f.b.

Urine. S.G. 1.010 to 1.018. N.P.N. 29 mgm. %.

Marked improvement after several days rest in bed. Gallop rhythm persisted for about ten days. Again left hospital against advice.

Third admission 3–16–34, just 2 weeks after his last discharge. Physical findings about the same as on previous admissions. Dyspnoea and oedema more marked. Protodiastolic gallop persistent. Course progressively down hill. Died 6–2–34, 10 weeks after his third admission.

Autopsy. Heart 645 grams. No valvular lesion. Coronary arteries smooth and delicate. No narrowing of the orifices. Rather diffuse scarring of the papillary muscles. Sections show marked scarring of the myocardium, the scars being associated with rather extensive infiltration of round cells. Lymphocytes scattered throughout the myocardium, especially about the small blood vessels. No typical syphilis of the aorta.

No arteriosclerosis of the kidneys or adrenals.

Case 5. H. Y. Colored male, aged 36.

Admitted 1–8–34, complaining of swelling of feet and shortness of breath. General health good until about 6 months before admission. Chancre 14 years before.

P. I. Dyspnoea on exertion for 6 months. Nocturnal dyspnoea and orthopnoea, 4 months. Went to hospital dispensary because of these symptoms and beginning palpitation. Found to have a positive Wassermann reaction and put on antisyphilitic therapy. Returned for treatment only twice. Forced to stop working about a month later. Oedema of feet and ankles for two weeks. Bloody sputum, one week. Some vague precordial discomfort.

P. E. Mild respiratory distress. No sclerosis of retinal vessels. Râles at both lung bases. Heart greatly enlarged to both right and left. No murmurs heard. Protodiastolic gallop rhythm, best heard at the apex. No evident sclerosis of peripheral vessels. B.P. 130/105. Liver 5 f.b. below costal margin. Marked oedema of lower half of body.

Wassermann positive. Urine: S.G. 1.017 to 1.029; no albumin, except for slight amount on admission. P.S.P. excretion 80% in two hours.

Systolic blood pressure varied between 140 and 105. Diastolic, between 105 and 90. Failed to improve with bed rest and digitalis. Died 5–23–34, four months after admission and less than a year after the onset of symptoms.

Autopsy. Heart 545 grams. No valvular lesion. Small areas of scar tissue throughout the left ventricle. A few fat deposits in aorta. Coronary arteries smooth and delicate. Sections show rather extensive scarring of the left ventricle.

Finer scarring of right ventricle. Scars infiltrated with lymphocytes. Clusters of lymphocytes around small blood vessels.

No sclerosis of arteries of kidneys, adrenals, or pancreas.

The blood pressures in these five cases are rather interesting in that they show the well recognized, but too often overlooked, effect of the failing right heart, with its resultant increased venous pressure, on the arterial pressure. In the four cases (1, 2, 3, and 5) with marked oedema of the lower half of the body and venous engorgement there were rather high diastolic pressures, but as the oedema subsided and the heart became compensated, the diastolic pressure fell. In the second case where there was marked oedema, hepatic enlargement, and ascites, the systolic pressure also was elevated and it, too, fell as the right heart became more able to carry its share of the circulatory burden. The patient (case 4) with only slight oedema of the ankles had diastolic pressures within normal limits.

These five cases present pictures resembling each other both clinically and pathologically. Clinically they could not be classified according to any of the usually accepted causes of heart disease. In none was there evidence of any organic valvular disease, nor was there any hypertension. Neither was there discernible nephritis, nor a history of anginal attacks, suggesting coronary arteriosclerosis. The absence of valvular disease and of coronary arteriosclerosis was confirmed at autopsy. The negative evidence of hypertension was supported by the condition of the arteries and arterioles of the kidneys, adrenals, and other organs at post-mortem examination. Pathologically, the only positive findings in the hearts were the extensive scarring of the heart muscle and the infiltration of the myocardium, endocardium and epicardium with round cells. These were not only the significant positive findings but they were common to the hearts in all five cases. All of the patients gave positive Wassermann reactions or had received antisyphilitic therapy.

The extensive round-cell infiltration and scarring of the myocardium suggest a chronic inflammatory process. There is evidence of no chronic infection, other than syphilis, in any of the cases.

It seems rather strange that there exists such marked difference of opinion as regards not only the frequency of the occurrence of syphilitic myocarditis, but also its actual existence. As early as

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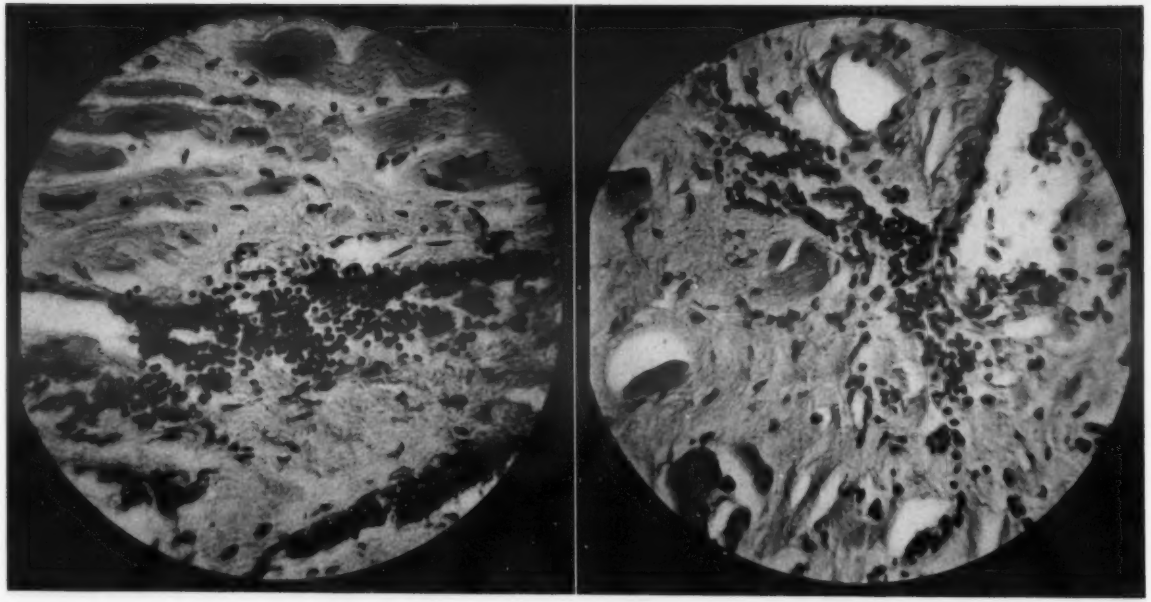

FIG. 1 FIG. 2

FIG. 1. TYPICAL MYOCARDIAL LESION SHOWING, IN THE CENTER, THE ROUND-CELL INFILTRATION; IN THE UPPER PART, THE DISINTEGRATING MUSCLE BUNDLES; AND IN THE LOWER PORTION, ADVANCED SCAR FORMATION

FIG. 2. A MORE ADVANCED STAGE OF THE SAME PROCESS WITH EXTENSIVE REPLACEMENT OF THE MUSCLE BY SCAR TISSUE
In the upper portion of the field are two blood vessels, neither of which show the least sign of sclerosis.

1914 Warthin (1) stated: "My own experience would make me believe that syphilis, both congenital and acquired, is the most important etiological factor in the production of cardiac disease, both myocardial and endocardial." In a series of reports between 1914 and 1930 (2, 3, 4, 5) he restated this position and presented considerable evidence to support it. Scott (6), Clawson and Bell (7), Saphir and Scott (8), Martland (9), and Saphir (10), take the view that the condition is very rare, if it exists at all. MacCallum (11), (in the 4th edition of his "Text Book of Pathology") is of the opinion that it occurs but seldom, while Boyd (12) is inclined to agree with Warthin. Although one cannot accept the latter's view that syphilis is the commonest cause of heart disease, one is forced to suspect that the condition is more prevalent than is generally admitted. Hamman and Rich (13) report in detail a case closely resembling those of this series and which they believe to be one of syphilitic myocarditis.

Most of the objections offered by those who believe that syphilitic myocarditis is infrequent are based on studies of hearts of individuals showing advanced syphilis of the aorta and aortic valve. That such studies may not be inclusive enough is suggested by the autopsied cases of the present study, none of which showed typical syphilis of the aorta. Also, in the 3000 cases reviewed there were 11 patients, less than 46 years of age, who came to autopsy showing definite syphilis of the aorta and the aortic valve. In only two of the eleven was there any pronounced infiltration of the myocardium with round cells—all of which would seem to suggest that, if this scarring and round-cell infiltration is syphilitic in origin, the condition may occur quite independently of syphilis of the aorta.

May these cases of unexplained cardiac failure be classified as syphilitic myocarditis? Thus far, the Levaditi and Warthin staining methods have not been successful in demonstrating the *Treponema* in the myocardium. However, much circumstantial evidence is available to support such a diagnosis. In the first place, there is no other plausible explanation; and it is striking that all of the patients gave serological evidence of syphilis. That of itself does not necessarily justify a positive Wassermann being accepted as an explanation for whatever cannot be explained by some other agent. But all five of these cases were in colored males—individuals notorious for their susceptibility to syphilis of the cardio-vascular system. The myo-

cardium of each showed marked infiltration of round cells throughout the scarred areas, between the muscle bundles, and around the smaller blood vessels. Such round-cell infiltration, especially when it is perivascular, is, in other parts of the body, generally accepted as being characteristic of syphilis. Why can it not be due to syphilis when it occurs in the heart muscle?

Rheumatic heart disease, probably the commonest form, easily distinguishes itself from the condition in question by both clinical and post-mortem findings. Clinically, it is frequently accompanied by evidence of organic valvular disease. It also demonstrates much more chronicity,—repeated attacks of decompensation over a period of years,—quite in contrast to the short history (usually less than two years) of cardiac trouble in the cases under discussion. The post-mortem findings are even more distinct, most cases of rheumatic disease showing definite endocarditis and the telltale Aschoff's bodies—the perivascular collections of large wandering cells, not at all likely to be confused with the round-cell infiltration of the present group of cases. The type of scarring in these cases is quite different from that of the rheumatic condition in that it is much more diffuse and frequently associated with areas of muscle necrosis.

SUMMARY

In 3000 admissions to the medical wards of the Baltimore City Hospitals there were 20 patients, all under 46 years of age, suffering from marked cardiac decompensation unexplained by any of the usually accepted causes of heart disease. These 20 cases seem to present a recognizable clinical group—marked cardiac enlargement, absence of evidence of organic valvular disease, absence of hypertension and general arteriosclerosis, low pulse pressure, and, invariably, protodiastolic gallop rhythms. All of these patients gave positive Wassermann reactions or had received anti-syphilitic therapy. Five of the twenty patients died and were autopsied. In none of these five was there any coronary arteriosclerosis, nor was there any valvular disease. Microscopically, all showed extensive scarring and round-cell infiltration of the myocardium. There was no sclerosis of the vessels of the kidneys, adrenals, or other organs to suggest the possibility that there had existed a previous hypertension.

CONCLUSION

Five cases of unexplained cardiac decompensation, all occurring in syphilitics, are presented with clinical and pathological findings. The picture presented by these cases—that of marked decompensation with no lesion other than diffuse scarring and round-cell infiltration of the myocardium—could well fit in with what would be expected of syphilis of the myocardium, and it is believed that the cases represent instances of syphilitic myocarditis.

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STUDIES ON VIRUS PROBLEMS[1]

III. The Elementary Bodies in Virus Infections and the Filterable Avian Tumors and Their Etiological Significance. The Outlook for the Future

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I propose in this last lecture to get down to more fundamental studies which have occupied my attention during the past three or four years and which bear on the biological nature of viruses. The outcome of this work has been to establish more firmly a contention, formerly based solely on inference from morphological observation and staining technique, that the bodies of uniform dimensions seen in suitably prepared material from virus lesions, particularly vaccinia and fowlpox, represent the actual virus agents. As you are aware, Borrel in 1904 observed minute bodies in enormous numbers in scrapings from fowlpox lesions, while in 1906 Paschen recorded the presence of similar small bodies in material from vaccinia and smallpox. The stain he used was steaming carbol fuchsin preceded by Loeffler's flagella mordant, a method which, in the hands of the experienced, is probably still one of the best and most certain, though now quite a number of new staining methods have recently been recommended. On this matter of staining I may say that whatever stain one uses, one must study and be familiar with all its pitfalls.

While these observations of Borrel and Paschen usually, though not invariably, received mention in current textbooks and monographs, little serious attention was paid to them for, I think, five and twenty years with the one exception perhaps of the ingenious experiments devised by Professor MacCallum and Miss Oppenheimer in 1922 for the separation and isolation of the infective granules in suspensions of calf lymph by spinning in fluids of varying specific gravity and

[1] Lecture III (abridged) of the Herter Lectures, The Johns Hopkins University. Delivered December 7, 1934.

testing systematically the deposits and supernatants on the rabbit cornea. The method has not been followed up, but the authors were able in this way to separate as the possibly infective agents granules which they identified with the Paschen bodies.

One reason for the neglect was the frequently expressed criticism, generally of workers who had no personal experience of their study, that these bodies were more likely to be stain artefacts or banal protein aggregates or anything but likely formed agents of disease. I commenced my study of these bodies about 6 or 7 years ago, when engaged on other work relating to vaccinia and fowlpox and I confess I approached their study with the sort of prejudice against their etiological importance which I had absorbed from the critics. The first difficulty to be overcome was to be satisfied that such bodies were really to be found in suitably stained material. Later the intention was to follow, if possible, the variations in their numbers and location in the course of the virus disease. The objective I always had in view, assuming I became convinced of the independent nature and possibly exogenous source of these bodies, was to be in a position ultimately to secure these bodies in pure suspension for crucial experiments, serological and etiological, but a few years elapsed before this desideratum was realised. My first study was to examine, by the mordanting method followed by carbol fuchsin, preparations from vaccinial lesions on rabbit skin at different periods after inunction of the virus, in order to see whether their numbers and location among the cellular elements of the lesion varied in any significant manner. This convinced me that any one proposing to take up the study of elementary bodies must serve a lengthy apprenticeship to the appropriate staining technique, in the course of which he will inevitably familiarise himself with the remarkably intriguing appearances that sheets and films of stain particles and protein aggregates may occasionally assume. This conviction I have repeatedly confirmed by observing the mistakes of junior colleagues approaching this study for the first time. Assurance, however, comes sooner or later, but in recording the definite presence of elementary bodies in any preparation I always adopt as a working rule the necessity of finding them in reasonably large numbers. The occasional elementary body seen in a preparation deserves little attention unless the previous content in elementary bodies of similarly

investigated material is high, as in fact it invariably is, in the initial stages of infection. In 1931 I was able to report that the elementary bodies of Paschen were demonstrable in large numbers about the 2nd or 3rd day in material from the rabbit lesion, and that investigation on subsequent days showed a very definite falling off in their numbers, the tendency being for the bodies to be congregated in the neighbourhood of cells of the lesion particularly the polynuclears. There was, therefore, a clear inference that, as the condition progressed, the elementary bodies, formerly demonstrable in large numbers and apparently lying free, became ultimately the prey of phagocytes after possibly undergoing agglutination. This I believe is what really happens, but, so far, the technical difficulties of demonstrating phagocytosis of elementary bodies by polynuclear cells have not been overcome, though I do not despair of this demonstration being achieved. If achieved and if it could be satisfactorily proved that elementary bodies, after sensitisation, became the prey of phagocytes, it would go far to explain the mechanism of the action of antiviral serum, as I suggested in my last lecture. Having then satisfied myself that these bodies in vaccinial lesions underwent variations in their numbers and distribution in the course of development of the lesion, my next objective was to obtain a pure suspension of these bodies from the raw material. This proved very difficult but ultimately, in 1931, I was able to report that by the use of ether and the centrifuge it is possible to separate sharply the epithelial and fattily degenerated polynuclear cells from the other constituents of the raw suspension. The great bulk of this lipoid material floats up with the ether to the top of the column leaving an opalescent fluid below. By centrifuging this subjacent fluid a deposit was obtained which was extremely rich in elementary bodies. Further fractional centrifugation, accompanied by tests of stained samples to assure myself that in the main only elementary bodies were present, resulted in the obtaining of a fairly pure suspension of Paschen bodies, which could be tested against the appropriate immune serum. The same technique proved readily applicable to fowlpox, indeed even more applicable, in view of the colossal numbers of Borrel bodies present in the epithelial lesions of fowlpox and the fact that epithelia containing Bollinger bodies readily break up in distilled water and ether and so discharge their content of Borrel bodies.

This method remains one of the best when the elementary bodies are required in large numbers in suspensions for serological work. With these suspensions of elementary bodies it has been possible to show that, in the animal infected with a single dose of virus administered by the intradermal route, agglutinins make their appearance in the blood serum about the 5th or 6th day, rise to a maximum and then slowly decline precisely like agglutinins arising in response to a dose of bacteria.

When one wants pure suspensions of elementary bodies for infectivity tests another technique must be used, because contact with ether has to be avoided. For this purpose, the raw virus roughly centrifuged is filtered through a Berkefeld V filter, followed by centrifugalisation of the filtrate at high speed. The centrifuge that has given good service in this field is one manufactured in Manchester, and of which I secured the first model three years ago. It develops a speed of 15,000 r.p.m. and half an hour or three quarters of an hour of such spinning is sufficient to throw down from a Berkefeld filtrate the great mass of the elementary bodies contained in it. By the aid of filtration and a centrifuge of this type it was now possible to investigate the infective properties of the elementary bodies. With my colleague Eagles a series of infection experiments was carried out with vaccinia filtrates and their washed deposits after centrifugalisation, which showed that a potent vaccinia filtrate could be completely depleted of infective power by the high speed centrifuge, while the deposit of elementary bodies thrown down from it and resuspended in saline proved alone to be infective. We drew the conclusion, which I think was well warranted, that the elementary bodies constituted almost certainly the virus agents and that any argument to the contrary would have to assume that the real virus was attached pretty firmly only to the elementary bodies in a raw suspension and, if so, it would have to explain exactly what the elementary bodies were if they were not the actual virus agents. I have so far heard of no reasonable alternative interpretation of this type of experiment, which I may say has been repeated and confirmed by Paschen and his colleagues in Hamburg.

The conclusion that the elementary bodies of vaccinia constitute the actual virus agents has also since been arrived at by Craigie of Toronto as the result of efforts to explain the flocculation reaction when specially

prepared virus suspensions of variola and vaccinia are mixed with antivaccinial serum. This phenomenon, as you are aware, was studied extensively by Gordon, and later by Tulloch and Craigie, and the test was recommended for the diagnosis of smallpox. Craigie has shown that the interaction taking place in this flocculation test is really due to one between a soluble substance derived in all probability from the elementary bodies and the antivaccinial serum.

I now pass to the application of this method to other viruses, variola, varicella and herpes zoster. With these, so far, my colleague Amies has worked and carried out serological tests of etiological bearing but, I believe, the number of viruses to which methods of this direct kind are applicable will prove to be very large. This is becoming clear from the estimates of size obtained from filtration and centrifuge data or even quite simply from the results of tests of infectivity of filtrate deposits obtained by high speed centrifugalisation. There would appear now to be a large range of viruses whose dimensions run from 100 mμ to 200 mμ and which in appropriately stained preparations can at any rate be detected if not completely resolved. Of these I might mention in addition to variola, vaccinia and fowlpox, varicella, herpes zoster, herpes labialis, psittacosis, ectromelia and molluscum contagiosum.

It seemed of first importance to investigate variola from this point of view and fortunately we had in England during many of these post-war years a considerable annual prevalence of the mild or alastrim type (though of late the prevalence has gone down to almost zero).

Material from variola minor was inoculated on the skin of the monkey, and an elementary body suspension was prepared from the monkey lesion. Also a suspension was made from the dermal reaction in the rabbit in response to variola virus. Some years ago I had shown that though, as is well known, variola material from man produces little or no reaction on the scarified skin of the rabbit, a reaction is invariably produced when the material is introduced into the dermis.

The interesting and surprising result with these sera from variola minor was that they produced little or no agglutination of the elementary bodies prepared from vaccinia, whereas a high proportion of them agglutinated readily the elementary bodies prepared from the variola material.

The agglutinins do not reach high titres but it is the exception in serological work with viruses to get high titres of antibodies. The fact that the serum of variola patients agglutinates variola elementary bodies but not those of vaccinia does not imply any complete divergence of antigen in the two cases. Monkeys infected with variola develop agglutinins for the elementary bodies of variola but not for vaccinia, whereas rabbits inoculated with material from these monkeys develop agglutinins both for variola and for vaccinia. All that can be said on this point at the moment is that variola and vaccinia share some common antigen and it must be left to absorption experiments—admittedly difficult experiments—to determine the precise change in antigen that takes place when variola assumes by passage the attenuated form of vaccinia.

Turning now to varicella, minute coccoid bodies were reported in varicella vesicles by Aragao, in 1911, and again apparently independently, in 1919, by Paschen, who suggested that they might be the actual infective agents. My colleague Amies went into this question and had no difficulty in demonstrating by appropriate staining methods the presence of elementary bodies in early vesicle fluid. His attempts to infect experimental animals proved unsuccessful. Occasional likely-looking reactions on the skin of the hamster gave some promise of successful initial transmission but passage was not obtained. Consequently, evidence for the etiological importance of these elementary bodies in varicella had to be sought by other means, and resort was had to the direct isolation of the elementary bodies from varicella vesicles. The fluid from the earliest vesicles was received into citrated saline to prevent clotting. This suspension was centrifuged first at low speed to throw down any gross debris. The supernatant was then transferred to a pyrex tube and spun at 12,000–15,000 r.p.m. The deposit of elementary bodies was taken up in 0.25 per cent formalin saline. The initial process is tedious, as many vesicles have to be pricked in order to get a sufficiency of elementary bodies to form a working suspension. It is most essential that only vesicles giving clear fluid be chosen. When the fluid is cloudy from the presence of inflammatory cells, the yield of bodies is very greatly diminished.

Agglutinins appear about 5 days after the onset of the eruption and persist for some time. Occasionally a case may show no development

of agglutinins, a circumstance which may possibly be correlated with known variations in the potency of convalescent measles and varicella sera as prophylactic agents.

In the diagnosis of doubtful cases of smallpox in which varicella may be suspected, the results of agglutination tests with the serum and suspensions of varicella and variola elementary bodies may be decisive.

Another direction in which research on the elementary bodies in virus disease has yielded fruitful results has been in establishing a long-suspected relationship between the viruses of varicella and herpes zoster.

Amies published a few months ago a series of comparative tests of varicella and herpes zoster sera with pure suspensions of elementary bodies from these viruses.

Clinical and epidemiological evidences of some intimate connection between these two diseases has been steadily accumulating for many years. The more usual sequence is for varicella to occur among contacts of a case of zoster, but there appear to be undoubted records of zoster following exposure to varicella. Evidence of connection has been sought so far by complement-fixation tests with varicella and zoster fluids. Paschen reported elementary bodies in zoster in 1933 and Taniguchi in 1934. Paschen also noted agglutination of elementary bodies when crude vesicle fluid was mixed with zoster convalescent serum. Amies collected 32 typical cases of zoster, of which 20 were seen at an early stage of the disease. Elementary bodies occur in great numbers in 24–48 hours after onset of vesiculation; later the bodies decrease and mononuclear cells appear. This cellular invasion occurs much later in zoster than in varicella. In films from the 4th day vesicle fluid bodies are often found lying clumped.

In all but two of 32 zoster patients, the sera agglutinated the corresponding elementary bodies, while 19 of them agglutinated also varicella elementary bodies. On the other hand, 5 out of 7 cases of varicella agglutinated the zoster elementary bodies.

OTHER PROPERTIES OF THESE ELEMENTARY BODIES

Do these elementary bodies retain their potency during storage? A study of this question by Amies has revealed the fact that when suspended in simple nutrient broth they can resist a temperature of 37°C.

for several weeks. At 0°C., as one might expect, little loss of potency occurs. These results made it worth while investigating how far such suspensions or rather dilutions of such suspensions were likely to be of value as a bacteria-free substitute for ordinary calf lymph in smallpox prevention. You are aware that Goodpasture has reported excellent results with stored virus prepared from growth in chick embryo in the egg, while Rivers has also prepared mass tissue culture virus as a substitute for ordinary calf lymph. The question is already being asked if these bacteria-free viruses are to have a future in smallpox prevention. Elementary body suspensions prepared by highspeed centrifugalisation of Berkefeld filtrates of vaccinia certainly represent the virus in its purest form and the technique of preparation is tolerably simple and straightforward. My colleague Eagles has been testing samples of elementary body suspensions stored in various menstrua for various perioas at 0°C. The complete data are not yet available for publication,[2] but already he has informed me that suspensions prepared from deposits of centrifuged filtrates of raw lapine suspended in broth have retained their potency unimpaired for 8 or 9 months. So also have suspensions in salt solution containing 0.5 per cent agar, but a menstruum of salt solution only has not been favourable to potency conservation. These samples give typical reactions on the rabbit both when rubbed on the freshly shaved surface and when inoculated intradermally. Time will show whether the days of calf lymph are numbered. I am unable at present to forecast future procedure in this important field.

THE FILTERABLE FOWL TUMOURS

During the past year I have, with the collaboration of Dr. W. E. Gye, made a preliminary study of the filterable avian sarcomata (Rous Chicken Tumour No. 1 and Fujinami's myxosarcoma) with a view to testing whether the technical methods discussed in this lecture were capable of being applied to the solution of the many problems surrounding the nature of these filterable agents. It has now emerged that high speed centrifugalisation of cell-free filtrates of these tumours depletes the filtrates of much of their potency and that, in the very

[2] See *Brit. J. Exp. Path.*, April, 1935.

small resulting deposits, the agent is concentrated in the form of elementary bodies of considerably smaller size than those of vaccinia. Suspensions of these bodies are also found to be agglutinated by the sera of tumour-bearing fowls. A new approach is thus opened up to the study of the agent responsible for these tumours. So far as the results go at present, they would support the view that the filterable "agent" is, at any rate in part if not in whole, extrinsic to the fowl. The question, however, how far isoantibodies may have to be considered and accounted for in serological work of this kind where fowls are concerned is one for further investigation (See *Lancet*. Feb. 16, 1935).

The Outlook for the Future

I have come now to the end of my talk on the particular virus problems which have most intimately concerned myself and my colleagues in recent years, and I only trust that in my enforced and often detailed allusions to these efforts I have managed to avoid giving the impression of unmindfulness of the virus field at large and of outside opinion at every point. Though I have discussed only a few problems I venture to think they are just those on which the fullest information is wanted if we are to make substantial progress in our real knowledge of viruses. In these days of rapid broadcasting of scientific information the discovery of some new virus by one worker is too often made the occasion for professional research workers elsewhere to step in and run through what is now an almost stereotyped gamut of experiment. The real enquirer, on the other hand, when he has exhausted this gamut, finds himself inevitably confronted with some fundamental virus problem which perhaps the peculiarities of the particular virus he is studying afford a fair chance of solving. This is the road to real advance. Now that there is some general agreement that many viruses are represented by visible and, shall I say, workable, elementary bodies, I conceive that advance in knowledge will be best served by concentrating on the agent itself and following its behaviour in the host and, if possible, in more artificial conditions outside the host. It will demand improved and possibly extremely difficult technique and no common fund of perseverance, but it is worth it for, where do we stand at the moment on one crucial question—are viruses independent living or multiplying agents?

The bacteriologist likes to see bacteria dividing on agar surfaces.

So far as this sort of evidence is concerned, I have on one occasion, in a preparation of Mr. Barnard, seen two canary-pox elementary bodies appear where there was only one before. Further, the psittacosis preparations of Professor Bedson undoubtedly suggest that a living and multiplying element is at work. The multiplication of virus that takes place in successful tissue culture, even though an increase in the number of elementary bodies can be demonstrated, does not, unfortunately, tell us that the elementary bodies used as seeding have independently multiplied. The critic can still argue that the virus body has, by its action on the cell, induced the latter to produce more of this substance. I feel, therefore, that further knowledge of this group of microscopically visible virus agents will come from following them up as such, by improving methods of culture and, if possible, by securing growth apart from the living cell.

When we come to consider viruses of the smallest dimensions, *e.g.*, between 100 mμ and 10 mμ such as poliomyelitis, louping-ill, foot and mouth disease and the plant mosaics, the problem of advance in knowledge of the agent seems at the moment more uncertain. If we take a haemoglobin molecule as possessing a diameter of 5 mμ, a virus of 20 mμ would contain say 60 protein molecules and one of 10 mμ, 9 protein molecules only. Speculation has been rife as to whether the metabolic activities of a living and multiplying agent are possible, given a complement of protein molecules of this low order. What prospects are there of advance in knowledge of these excessively minute agents? Respiration studies in tissue culture may help us much. It is surprising how little this field has been worked. The centrifuge of the high speed type may, however, again come to our assistance. The ordinary high speed centrifuge running at say 15,000 r.p.m. or a little more is not likely to be helpful unless perhaps it can be adapted to long periods of running without injury to the virus. On the other hand, the Svedberg velocity centrifuge running at speeds of 60,000–90,000 r.p.m. may find useful application in the virus problems we are considering. With its photographic recording equipment it may be possible to watch the deposition of virus bodies as distinct from that of the protein molecules with which the virus is inevitably associated. I trust that this remarkable tool, which in the hands of Svedberg has been of such service to physical and colloidal chemistry, may become available for service in the virus field.

BOOK REVIEWS

(These reviews represent the individual opinions of the reviewers and not necessarily those of the members of the Editorial Board of this journal.)

The Principles and Practice of Nursing. By BERTHA HARMER. 1934. 2nd edition. 845 pp. Illust. $3.00. (*Macmillan Co., New York.*)

This revised edition is significant of the viewpoint of modern nursing. The author has stressed health and preventive aspects, the fact that mental and physical health are closely interdependent, and that in the family and social life of individuals there are potent contributing factors to the prevalence of mental and physical ill-health which, even in hospitals, still exist for the patient and have a powerful influence on his recovery.

Much of the text has been rewritten, new illustrations have been added and new methods of treatment discussed. The postoperative care of neuro-surgical patients has been included under the chapter dealing with treatment following special operations.

The book should be of invaluable assistance to teachers of practical nursing work as well as to their students.

V. B.

Allergy and Applied Immunology. A Handbook for Physician and Patient, on Asthma, Hay-fever, Urticaria, Eczema, Migraine and Kindred Manifestations of Allergy. 1934. 2nd edition. 420 pp. $5.00. (*C. V. Mosby Co., St. Louis, Mo.*)

The author has made a brave attempt to present simply, for the edification of the layman, a subject still rife with many theoretical problems.

Exclusion of much that is still controversial in the allergic field, and simplification of a complicated nomenclature, would add greatly to the author's purpose. The text is much too complicated even for a very intelligent layman.

W. L. W.

Physical Diagnosis. By WARREN P. ELMER and W. D. ROSE. 1935. 7th ed. Illust. 919 pp. $8.00. (*C. V. Mosby Co., St. Louis, Mo.*)

If the reviewer's memory is correct, this modification of Rose's Physical Diagnosis is marked by a substantial elaboration and improvement in all departments of the subject. Pure physical diagnosis is amplified by excellent sections on electrocardiography by Dr. Drew Luten and on roentgenology by Dr. Sherwood Moore. One of the most valuable features is the illustrations: anatomic outlines and the location and propagation of various phenomena concerned in physical diagnosis are projected to the surface in remarkably satisfactory delineations.

The book is almost an ideal textbook, but certain statements that are more or less traditional but that are, nevertheless, open to more than doubt might be mentioned. For example: "Pulsation in the episternal notch attends simple dilatation of the aorta or aneurysm with great constancy." This fact suggests to the reader that such pulsation (in reality, due to the innominate artery in most instances) is caused by a palpable pulsation of the aorta or of an aneurysm, and the statement deserves amplification. A more detailed description of jugular pulsations, as seen by the naked eye, though well described in polygraphic tracings, would be valuable. The authors give the traditional description of egophony, as being heard just *above* the level of thoracic fluid. The reviewer always hears egophony everywhere over a substantial effusion, diminishing but still audible quite to the diaphragm: the authors would present a step forward in physical diagnosis if they would prosecute this point further. The reviewer can see nothing but error in the statement on page 454 that "With the inception of auricular fibrillation the murmur of mitral stenosis is abolished."

The dedication to Dr. George Dock is appropriate and indicates the esteem in which he is held by his associates and his influence on medicine in this country.

J. T. K., Jr.

Psycho-Analysis for Teachers and Parents. Introductory Lectures. By Anna Freud. [Translated by Barbara Low.] 1935. 117 pp. $1.75. (*Emerson Books, Inc., New York.*)

The daughter of Sigmund Freud presents four chapters dealing with the theories of psycho-analysis and its relations to pedagogy. These concise and lucid lectures may well serve as an introduction to Freudian psychology for the interested student and practitioner of medicine.

J. H. C.

Microbiology and Elementary Pathology. For the Use of Nurses. By Charles G. Sinclair. 1934. 102 illust. 377 pp. $2.75. (*F. A. Davis Co., Phila., Pa.*)

This second edition of the book, first published in 1931, shows only slight changes in the section on Microbiology. A new chapter has been added on "Pathological Chemistry."

A very useful book, giving a brief but clear presentation of the knowledge a nurse should acquire about these subjects.

L. E. K.

The Principles of Treatment of Muscles and Joints by Graduated Muscular Contractions. By Morton Smart. 1933. 218 pp. $3.75. (*Oxford Univ. Press, New York.*)

This is a résumé of the general physiology of muscle posture and muscle mechanics. The author notes the pathological changes caused by injuries to the muscles and joints and considers seriatim sprains and strains, the manipulative

treatment of the shoulder-joint crippled by adhesions, the treatment of muscle and joint trauma and other selected conditions, by the use of graduated muscle contractions.

It is claimed that early normal function is obtained, adhesions are prevented, and oedema and haemorrhage are rapidly absorbed as a result of the increase in the blood supply engendered by these contractions.

M. B. S.

The Art and Principles of Nursing. By AMY E. POPE and VIRNA M. YOUNG. 1934. 832 pp. $2.75. (*G. P. Putnam's Sons, New York.*)

This is a revision of "Practical Nursing" by Maxwell and Pope, the latest edition of which appeared in 1923.

In some places a marked improvement has been effected by a thorough reorganization of material. In others the text has been revised to conform to present-day teachings in anatomy and physiology.

The authors have described many methods of carrying out the various nursing procedures and given considerable space to the use of tests and other diagnostic measures. They have, however, paid very little attention to the social and public health aspects of nursing.

The book will be more valuable for reference than as a text for elementary students.

E. N.

The Clinical Aspects of Visceral Neurology. With Special Reference to the Surgery of the Sympathetic Nervous System. By W. K. LIVINGSTON. 1935. 254 pp. $5.00. (*Chas. C. Thomas, Springfield, Ill. and Baltimore.*)

This is a very timely book. It is devoted to a clinical consideration of a few of the many diseases for which sympathectomy has been advised. An earnest effort has been made to eliminate the many vague and unsupported theories which abound in this field and to deal only with fairly well established facts. Very brief discussions are given of the anatomy and physiology of the visceral nervous system. The author then describes the essential symptoms of a number of clinical conditions, such as Raynaud's disease, thromboangitis obliterans, Hirschsprung's disease, angina pectoris, erythromelalgia, hypertension, etc. The various methods of diagnosis required in the selection of cases for operation are given in full and the surgical technique and various types of operation are discussed. The author's personal experience and a number of case reports are included. The book displays a great deal of sound judgment and common sense, and may be recommended to anyone interested in this field.

F. R. F.

The Nervous Patient. By CHARLES PHILLIPS EMERSON. 1935. 453 pp. $4.00. *J. B. Lippincott, Phila., Pa.*

The problems of the "functional physical and mental states" are presented from

the viewpoint of the internist. The rôle which the emotions and personality patterns play in somatic disease is carefully evaluated. The disorders of the sex life are discussed in line with Freudian conceptions. The book is a well organized attempt to correlate general psycho-pathology with practical medical problems. J. H. C.